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10/517,077	06/01/2005	David Duncan Heath	JAMES68.008APC	8641

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EXAMINER	
BERRIOS, JENNIFER A	

ART UNIT	PAPER NUMBER
1619	

NOTIFICATION DATE	DELIVERY MODE
05/26/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/517,077	HEATH, DAVID DUNCAN	
	Examiner	Art Unit	
	Jennifer A. Berríos	1619	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 February 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10 and 31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10, 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to the reply filed on 2/24/2010.

Currently claims 1-10 and 31 are pending examination.

Maintained Rejections

Claim Rejections - 35 USC § 103

1. Claim 1-9 **remain** rejected under 35 U.S.C. 103(a) as being unpatentable over Hashimi et al (WO 01/07079, pub date: 2/1/2001), Tamura et al (Immunology (1975) Vol. 28, No. 5, pg 909-924) and Folds et al (Journal of Clinical Microbiology, Aug 1983, Vol. 18, pg 321-326).

Regarding claims 1-3 and 5-9, Hashimi teaches a vaccine formulation providing for the extended release of antigenic material over time. The release profile of the different embodiments can be varied, allowing a single administration to establish active immunity in an animal (Abstract). The antigenic material will be released from the carrier system over a period of time after introduction of the vaccine into the subject (Pg 3, lines 25-26). The at least one antigenic substance will be dispersed in a pharmacologically acceptable carrier (Pg 20, claim 1). Hashimi contemplates periodically supplementing a relatively constant rate with burst of higher release, used to trigger the immune system to remain highly active over time (Pg 10, lines 7-10). It is also suggested that the shape of the device can be chosen to affect both the initial release rates and the effect of any tailing off thereof (Pg 12, lines 23-25). .

A further variation is for the device to have multiple layers, or graduated layers. This allows for differing release rate profiles merely by adding layers of different

solubility and/or release rates, or containing different concentrations of active material. (Pg 12, lines 26-29) Hashimi further teaches that the vaccine delay can exceed 24hrs and also 5days (Pg 21, claim 15-16).

While Hashimi teaches increasing release profiles and varying concentrations of pharmaceutical agents in a single vaccine administration, Hashimi fails to teach increasing dose.

Tamura teaches cellular and humoral immune responses in mice and teaches that the anti TNP antibody production was maximally enhanced by presensitization with a low dose of SRBC and gradually abolished with higher does of SRBC for pre sensitizations. In the latter case, anti SRBC antibody production was increased with increasing doses of SRBC (Abs).

Folds teaches purified Rickettsia rickettsii vaccine evaluated in guinea pig models. Guinea pigs were partially protected by the vaccine when challenged with virulent, viable rickettsiae. However, greater protection was observed when higher doses of vaccine were given and when frequent booster injections were administered (Abs).

It would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Hashimi, Tamura and Folds to increase doses of a pharmaceutical agent in a single, administratable composition. One of skill in the art would have been motivated to utilize the vaccine formulation device of Hashimi, having different release rate and concentration profiles, to create a formulation with increasing doses to ensure greater protection and higher antibody production.

Further, one of ordinary skill in the art at the time the invention was made would have been motivated to increase dosages, taught by Tamura and Folds, in the single formulation of Hashimi, to eliminate multiple administrations, resulting in greater patient compliance and health care efficiency. Finally one of skill in the art would have had a reasonable expectation of success for combining increased doses of Tamura and Folds in the single vaccine formulation of Hashimi because Hashimi teaches increasing release rates and varying concentrations of pharmaceutical agents in a layered configuration within a single composition, see pertinent page and line numbers) and Tamura/Folds teach increased immunogenicity and protection with vaccine formulations administered with increasing doses.

Response to Arguments

Applicant asserts that none of the cited references teach progressively increasing doses of one or more biologically active agents.

Applicant's assertion has been fully considered, but is found unpersuasive since Tamura explicitly teaches on page 913 (emphasis added):

"…anti-SRBC antibody responses were heightened with ***increase in dose of*** carrier SRBC."

With regard to the teachings of Tamura, applicant points out that Tamura is solely interested in the effect of responses to injection of a hapten-conjugated SRBC carrier when the carrier is intraperitoneally or subcutaneously injected with SRBC carrier

alone. Applicant argues that Tamura does not teach progressively increasing doses of the biological agent of interest.

Applicant's arguments regarding the teachings of Tamura have been fully considered, but are found unpersuasive. Since SRBC clearly develops an antibody response in mice, the SRBC carrier is an antigen in mice. Tamura explicitly demonstrate increased antibody titer to SRBC in response to increased doses of the SRBC antigen, see Figures 3a, 5, 6 and the last paragraph on page 923. Therefore, regardless of the thrust of Tamura's investigative interests, Tamura clearly teach "progressively increasing doses of doses of said one or more biologically active agents", as required by instant claim 1.

With regard to the teachings of Folds et al., applicant argues that Folds et al. also fails to teach the progressively increasing doses of the present application's claims.

Applicant's arguments have been fully considered, but are found unpersuasive. Progressively increasing doses is not required to be taught by Folds et al. since this limitation was satisfied by the teachings of Tamura et al.

Applicant further argues that in contrast to the instant claims, Folds et al. examined the effects of an initial dose of either 0.5 ml of a 1:3 dilution or 0.5 ml of a 1:100 dilution of vaccine in separate sets of guinea pigs, followed by booster injections of the same dose.

A review of Folds et al. has been fully considered, but is still applicable against the instant claims. Folds et al. clearly demonstrate protective efficacy of a vaccine administration with repeated administrations, providing evidence of motivation for

providing multiple doses of the same antigen within the single dose configuration of Hashimi. Further, Folds clearly demonstrate better vaccine protection when higher doses of the vaccine and boosters are administered, see Tables 1, 2 and 5 for example.

It is maintained that the combination of Hashimi/Tamura and Folds would have motivated one of skill in the art to create a formulation with increasing doses to ensure greater protection and higher antibody protection. Furthermore, increased dosages in a single administration would eliminate the need for multiple administrations, thus resulting in greater patient compliance and health care efficacy.

2. Claim 10 and 31 **remain** rejected under 35 U.S.C. 103(a) as being unpatentable over Hashimi et al (WO 01/07079, pub date: 2/1/2001), Tamura et al (Immunology (1975) Vol. 28, No. 5, pg 909-924) and Folds et al (Journal of Clinical Microbiology, Aug 1983, Vol. 18, pg 321-326), as applied to claims 1-9 above, and further in view of Sako et al (WO 94/06414, pub. date: 3/31/1994)

For ease of examination, the Examiner relied upon US Patent 6,436,441 as an equivalent English translation of the Japanese WO 94/06414 publication. All citations henceforth to Sako are locations in the US Patent.

Sako teaches a hydrogel-type sustained release preparation comprising at least one drug. Fig. 10 demonstrates different plasma drug concentrations having a progressively increased dosage around 2 hrs.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teaching of Hashimi/Tamura/Folds and Sako. While Hashimi, Tamura, Folds and Sako do not specifically teach doubling the dose or

the specific incremental concentrations of agents instantly recited in claims 4, 10 and 31, manipulation of relative amounts of formulation components resulting in differences in concentration will not support the patentability of subject matter encompassed by the prior art, unless there is evidence indicating that such concentration data is critical. "[W]here the general conditions of a claim are disclosed in prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). The adjustment of particular conventional working conditions as well as affecting the desired therapeutic effect, is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan. Accordingly, this type of modification is no more than an effort to optimize results. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results to the contrary.

Response to Arguments

Applicant argues that Sako does not cure the deficiencies of Hashimi/Tamura and Folds.

Applicant's arguments have been dully considered, but are found unpersuasive since there are no deficiencies in the combined teachings of Hashimi, Tamura and Folds to cure.

Conclusion

1. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer A. Berríos whose telephone number is (571)270-7679. The examiner can normally be reached on Monday-Thursday: 7:00am-4:00pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (571) 270-0871. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jennifer A Berríos/
Examiner, Art Unit 1619

/Shanon A. Foley/
Primary Examiner, Art Unit 1619